Remarks

Claims 1-20 and 25-31 are pending with claim 1 being independent. Claims have been amended and claims have been added. Support for the addition of "oral administration" of the fast-dissolving tablets of the claims is found, for example, at page 2, lines 30-31 of applicants' disclosure. Support for the addition of "one or more drugs" acting as COX-2 inhibitors is found, for example, in applicants' claim 1 as filed, at page 4, lines 6-12 of applicants' disclosure. Support for the addition of "croscarmellose sodium" is found, for example, at page 5, lines 24-25 of applicants' disclosure. Support for "one or more pharmaceutically acceptable excipients, wherein at least one of the pharmaceutically acceptable excipients comprises a filler" is found, for example, at page 4, lines 19-31. No new subject matter has been added by these amendment or new claims.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1-20 have been rejected as indefinite for allegedly failing to state the amount of COX-2 inhibitor present in the formulations, for allegedly failing to state the amount of filler or binder mannitol, and for allegedly failing to state the amount of lubricant or glidant talc. Applicants respectfully traverse the rejection for the following reasons.

As there is no per se requirement for a pharmaceutical formulation to specify exactly the amount of a pharmaceutically active ingredient, or excipient, applicants submit that the claims are not indefinite as presented. Further, applicants point out that claim 1 specifies a "therapeutically effective amount of one or more drugs that act as a ... COX-2 inhibitor..." Thus, applicants respectfully request reconsideration and withdrawal of the rejection.

Objection

Claim 7 has been objected to for depending from claim 9. The dependency has been corrected, and claim 7 now depends from claim 1, properly.

Rejection Under 35 U.S.C. 102(b) Over Humber et al. (EP 748 628 A2)

Claims 1-19 have been rejected as anticipated by Humber et al. Applicants respectfully traverse the rejection for these reasons.

Humber et al. discloses novel formulations of etodolac, in particular, organoleptically acceptable oral formulations of S(+)-etodolac. Humber et al. discloses excipients generally for use in such formulations at page 4, lines 6-11,

("pharmaceutically acceptable excipients, fillers, diluents, lubricants, disintegrants, suspending or stabilizing agents, and binding agents including, but not limited to, magnesium stearate, sodium lauryl sulfate, microcrystalline cellulose, polyvinylpyrrolidone, gelatin, alginic acid, acacia gum, sodium citrate, complex silicates, calcium carbonate, glycine, dextrin, sucrose, sorbitol, dicalcium phosphate, calcium sulfate, lactose, kaolin, mannitol, sodium chloride, talc, dry starch (e.g., corn, potato or tapioca starch) and powdered sugar."

Humber et al. does not disclose croscarmellose sodium in their formulations, neither in the general description, nor in any specific example. Humber et al. goes on to describe various excipients for use in formulations for use in various applications such as oral liquid formulations (Examples 1 and 2), chewable tablets (Examples 3 and 23, and description, page 6, lines 30-33), effervescing powders (Examples 4-8, and description, page 7, lines 6-25), effervescent granules (Example 9), rapidly disintegrating solid dosage forms (Examples 10-15), buccal formulations (Example 15), lozenge or troche formulations (Example 16 and description, page 11, lines 9-10), dentifrice compositions (Examples 17 and 18, and description, page 12, lines 12-24), chewing gum (Example 19), veterinary formulations (Example 20-22). Nowhere in this extensive disclosure is croscarmellose sodium mentioned.

The presently claimed invention calls for croscarmellose sodium, and thus Humber et al. does not anticipate the claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection Under 35 U.S.C. §103(a) Over Humber et al.

Claims 1-19 have been rejected as obvious over Humber et al. Applicants respectfully traverse the rejection for the following reasons.

As discussed above, Humber et al. does not disclose croscarmellose sodium anywhere in the reference. Further, there is no suggestion or teaching to use croscarmellose sodium anywhere in the reference.

Croscarmellose sodium is a crosslinked polymer of carboxymethylcellulose sodium. Humber et al. does not disclose the use of any crosslinked polymeric material for the formulations described in the reference. Thus, there is no motivation to use a crosslinked polymeric material in the formulations of Humber et al. Further, although Humber et al. does disclose the use of sodium carboxymethylcellulose in Examples 1 and 2 for liquid oral formulations, and in Examples 17 and 18 for dentifrice compositions, it is described as a suspending agent (page 4, lines 33-34). The rapidly disintegrating solid dosage formulations disclosed in Examples 10-15 do not use crosslinked polymeric ingredients, as mentioned above, and do not use carboxymethylcellulose sodium.

Thus, applicants submit that there is no motivation to employ a crosslinked carboxymethylcellulose sodium in the formulations of Humber et al. A *prima facie* case of obviousness has not been made out. Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection Under 35 U.S.C. §103(a) Over Humber et al. and Plachetka (United States Patent No. 6,586,458)

Claim 20 has been rejected as obvious over Humber et al. in view of Plachetka. Applicants respectfully traverse the rejection for the following reasons.

As discussed above, Humber et al. does not disclose, teach or suggest the use of croscarmellose sodium in any of their formulations, much less in rapidly disintegrating tablet formulations such as those of the present invention. Plachetka discloses examples of rapidly dissolving tablets including pharmaceutical agents which are NSAIDs (ergotamine tartrate, naproxen sodium, and sumatriptan), but which are not COX-2 inhibitors, and states "[o]ther agents may also be present such as: pregelatinzed maze [sic] starch, polyvinyl-pyrrolidone or hydroxypropyl methylcellulose; fillers (e.g., lactose, microcrystalline cellulose or calcium phosphate); disintegrants (e.g., potato starch, crocarmellose sodium, or sodium starch glycolate); wetting agents (e.g., sodium lauryl sulphate) or other agents for tabletting" (col. 10, lines 61-67). Thus, the exemplified rapidly disintegrating tablets of Plachetka do not include COX-2 inhibitors as pharmaceutically acceptable agents. Applicants submit that the Examiner has used hindsight reconstruction, with applicants' disclosure as a road map, to recreate combinations of elements in the prior art, to correspond to applicants' claimed invention. Such hindsight does not constitute a *prima facie* case of obviousness.

Further, nowhere does Plachetka disclose or suggest that the rapidly disintegrating tablets can be prepared by direct compression, as set forth in applicants' new claim 29.

Thus applicants submit that the claims as presented herein are allowable, and respectfully request a Notice of Allowance as the next paper from the Office.

Respectfully submitted,

MURPANI et al.

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Date: March 26, 2004

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aluminium hydroxide, magnesium silicate, aluminium magnesium hydroxide, maltose, maltitol, sorbitol, mannitol, glucose, sucrose, xylitol, lactose, lactose monohydrate, erythritol, fructose, maltodextrins, microcrystalline cellulose, calcium carboxy methyl cellulose, pregelatinized starch, potato starch, maize starch, kaolin, polyethylene glycol 4000, and mixtures thereof.

8. (currently amended) The tablet according to claim 1 ~~2~~ wherein the one or more pharmaceutically acceptable ~~pharmaceutical~~ excipients comprises one or more of binders, disintegrants, lubricants, glidants, colouring agents, flavouring agents and sweeteners.

9. (currently amended) The tablet according to claim 8 wherein the binders is ~~may be~~ selected from the group consisting of microcrystalline cellulose, mannitol, microcrystalline dextrose, directly compressible dicalcium phosphate, amylose and polyvinylpyrrolidone.

10. (original) The tablet according to claim 8 wherein the disintegrant is selected from the group consisting of starches or modified starches, clays, celluloses, algins, cross-linked celluloses, gums, cross-linked polymers, effervescent agents, and mixtures thereof.

11. (original) The tablet according to claim 10 wherein the disintegrant is selected from the group consisting of sodium starch glycolate, corn starch, potato starch, pregelatinized starch, bentonite, montmorillonite, veegum, microcrystalline cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, sodium alginate, alginic acid, croscarmellose sodium, guar gum, xanthan gum, crospovidone; sodium bicarbonate and citric acid, and mixtures thereof.

12. (currently amended) The tablet according to claim 8 wherein the lubricant is ~~lubricants may be~~ selected from the group consisting of talc, magnesium stearate, calcium stearate, stearic acid, magnesium lauryl sulphate and hydrogenated vegetable oil, sodium

benzoate, sodium acetate, sodium chloride, leucine, sodium stearyl fumarate, PEG 4000, and mixtures thereof.

13. (currently amended) The tablet according to claim 8 wherein the glidant is ~~glidants may be~~ selected from the group consisting of colloidal silicon dioxide and talc.

14. (currently amended) The tablet according to claim 8 wherein the colouring agent is ~~agents may be~~ selected from any pharmaceutically acceptable colorant ~~used in pharmaceuticals which is approved and certified by the FDA~~.

15. (currently amended) The tablet according to claim 8 wherein the flavouring agent is ~~may be~~ selected from the group consisting of natural and artificial flavours, mints and essential oils and ~~or the~~ mixtures thereof.

16. (currently amended) The tablet according to claim 15 wherein the flavouring agent is ~~may be~~ selected from the group consisting of peppermint, menthol, artificial vanilla, cinnamon, various fruit flavours, both individual and mixed, thymol, eculyptol and methyl salicylate and mixtures thereof ~~the like~~.

17. (currently amended) The tablet according to the claim 8 wherein the sweetener is ~~may be~~ selected from the group consisting of natural and artificial sweeteners.

18. (currently amended) The tablet according to the claim 17 wherein the sweetener is ~~may be~~ selected from the group consisting of monosaccharides, disaccharides, polysaccharides, partially hydrolyzed starch, corn syrup solids, sugar alcohols, water-soluble artificial sweeteners, and mixtures thereof.

19. (original) The tablet according to the claim 18 wherein the sweetener may be selected from the group consisting of xylose, ribose, glucose, mannose, galactose, fructose, dextrose, sucrose, maltose, sorbitol, xylitol, mannitol, soluble saccharin salts,

cyclamate salts, acesulfam-K and free acid form of saccharin and dipeptide based sweeteners, and mixtures thereof.

20. (currently amended) ~~A mouth~~ An orally administered, fast dissolving tablet comprising ~~of COX-2 inhibitor consisting of~~ a COX-2 inhibitor, croscarmellose sodium, mannitol, aspartame, colloidal silicon dioxide, magnesium stearate and one or more flavouring agents ~~agent~~.

21. (withdrawn) A process for preparing a fast dissolving tablet according to claim 2 comprising the steps of:

(a) blending a therapeutically effective amount of COX-2 inhibitor, a filler, and optionally, other pharmaceutical excipients;

(b) compressing the homogeneous mixture obtained in step (a).

22. (withdrawn) The process according to claim 21 wherein the blend is granulated before compression.

23. (withdrawn) The process according to claim 22 wherein the granulation is done by wet or dry granulation methods.

24. (withdrawn) The process according to claim 23 wherein the dry granulation is done by slugging or roller compaction.

25. (new) The tablet according to claim 1 wherein the one or more drugs that act as a cyclooxygenase-2 (COX-2) inhibitor comprises about 1% to about 90% w/w of the tablet.

26. (new) The tablet according to claim 8 wherein the binder comprises about 1% to about 10% w/w of the tablet.

27. (new) The tablet according to claim 8 wherein the lubricant comprises about 0.25% to about 4% w/w of the tablet.

28. (new) The tablet according to claim 8 wherein the glidant comprises about 0.1% to about 10% w/w of the tablet.

29. (new) The tablet according to claim 1 wherein the tablet is prepared by direct compression.

30. (new) The tablet according to claim 5 wherein the tablet comprises between about 2.5 mg and about 100 mg of rofecoxib per tablet.

31. (new) The tablet according to claim 1 wherein the tablet dissolves in the mouth

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